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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
4173	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,152	HAAPALINNA ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *9 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sheet (1)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-15 are currently pending in the application.

Applicant's election with traverse to the lack of unity invention in the reply filed on 11/30/07 is acknowledged. The traversal is on the ground(s) that Box IV of the PCT written opinion dated January 26, 2004, for the international application PCT/FI03/00240 was not checked and that Examiner conclusion about the special technical feature being drug abuse is erroneous. This is not found persuasive because the claims as recited in the instant application before the election/restriction requirement denoted a method for the treatment of physical dependence and/or one or more withdrawal symptoms utilizing a selective alpha-2-adrenoceptor antagonist which was known in the art at the time of the invention. Examiner interpreted the physical dependence as drug abuse given that drug dependence is characterized by physical dependence and absent of a clear definition of physical dependence by applicant in the disclosure, claims are given their broadest reasonable interpretation. In fact, the Merck Manual characterized physical dependence as a concept that encompasses both drug dependence and tolerance (see Merck Manual, pg.1 lines 2-3). Moreover, the Merck Manual further suggests that drug abuse involves dependence (Merck Manual, pg. 1, last paragraph). As a result, physical dependence is considered to encompass drug abuse and as such Examiner concluded that the method of treatment of drug abuse and/or withdrawal symptoms comprising a selective alpha-2-adrenoceptor antagonist is

the common special technical feature that is disclosed by Seiler (U.S. Patent 7,012,085 B2). Thus, in this instance, these inventions as presented do not make a contribution over the prior art with respect to novelty and inventive step and therefore lack unity. It is further noted that a lack of Unity of Invention is different from restriction practice in the U.S. in some major aspects. Unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371. Restriction practice, however, applies to U.S. national applications filed under 35 U.S.C. 111(a), even if the application filed under 35 U.S.C. 111(a) claims benefit under 35 U.S.C. 120 and 365(c) to an earlier international application designating the United States or to an earlier U.S. national stage application submitted under 35 U.S.C. 371. Consequently, the checking of box IV of the PCT written opinion has no bearing on examination practices in the U.S.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 9 and 11-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating one or more withdrawal symptoms caused by the discontinuation of the use of at least one psychostimulant agent in a mammal, which comprises administering to the mammal an effective amount of a selective alpha-2-adrenoceptor antagonist, does not reasonably provide enablement for a method to prevent the aforementioned conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. For example, after chronic drug abuse, patients typically develop withdrawal symptoms, a central nervous system response to the dependence on the drug (see J. of Psych. 1998, pg. 231, paragraph 3). Consequently, prevention of withdrawal symptoms regardless of the severity is unlikely.

The instant claim is drawn to a method of treating one or more withdrawal symptoms caused by the discontinuation of the use of at least one psychostimulant agent in a mammal, which comprises administering to the mammal an effective amount of a selective alpha-2-adrenoceptor antagonist. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention.

Attention is directed to *In reWands,* 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman,* 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Specifically, in regard to the breadth of the claims, the predictability of the art, and the amount of guidance of direction, claim 3 fails to embrace and read on preventing one or more withdrawal symptoms caused by the discontinuation of the use of at least one psychostimulant agent in a mammal, which comprises administering to the mammal an effective amount of a selective alpha-2-adrenoceptor antagonist set forth in the instant specification.

Since the instant specification provides no limiting definition of the term "prevention", the examiner will adopt the broadest reasonable interpretation for same. Webster's Ninth New Collegiate Dictionary defines "prevention" as "to keep from happening or existing", i.e., to completely eradicate.

The claim is thus very broad insofar as they recite the "prevention" of withdrawal symptoms, i.e., the complete eradication of same. While such "prevention" might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the "real world" in which patients live.

As for the guidance of the specification as to the prevention of one or more withdrawal symptoms, the above is severely limiting given that the specification provides no direction or guidance for prevention of one or more withdrawal symptoms despite the prior art disclosing that withdrawal symptoms do occur. No reasonably specific guidance is provided concerning useful therapeutic protocols for such prevention.

As for the predictability of the art, Murray specifically pointed out that after discontinuation of drugs such as amphetamines, withdrawal symptoms such as paranoia develop within three to four hours. Consequently, the predictability in the art is high.

In conclusion, the applicant is enabled for a method of treating withdrawal symptoms,, but not for the prevention of such condition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Seiler et al. (U.S. 7,012,085 B2) as evidenced by Murray (J. of Psych. 1998, Vol. 132, No.2, pgs. 227-237).

Specifically, Seiler et al. discloses a method of treatment using an alpha-2-adrenoceptor antagonist for depression and drug abuse (see claim 6-col. 12). In addition, these alpha-2-adrenoceptor antagonists are able to inhibit amphetamine induced symptoms such as ambulatory activity, depression and drug abuse (see col. 3, lines 55-61 and lines 66-67; col. 4, lines 1-15). Finally, Seiler discloses that these antagonists can be administered in large mammals such as humans (see col. 4, lines 23-24).

Accordingly, the teachings of Seiler et al. anticipate claims 1-2 and 6-8.

Murray discloses that amphetamines can produce depression (pg. 228) and is accompanied by withdrawal effects, an inherent consequence of the chronic drug use (pg. 230, 2nd and 3rd paragraph). Murray further discloses that complete discontinuation of amphetamines leads to clinical depression (pg. 230, 4th paragraph). Murray has been provided to show that chronic use of psychostimulants such as amphetamines is associated with withdrawal symptoms and can lead to depression upon discontinuation. Consequently, Seiler teaches a method of treating withdrawal symptoms as evidenced by Murray using alpha-2-adrenoceptor antagonists.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 and 6-8 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Seiler et al. (U.S. 7,012,085 B2) in view of Murray (J. of Psych. 1998, Vol. 132, No.2, pgs. 227-237).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Seiler et al. teaches a method of treatment using an alpha-2-adrenoceptor antagonist for depression and drug abuse (see claim 6-col. 12). In addition, these

alpha-2-adrenoceptor antagonists are able to inhibit amphetamine induced symptoms such as ambulatory activity, depression and drug abuse (see col. 3, lines 55-61 and lines 66-67; col. 4, lines 1-15). Finally, Seiler teaches that these antagonists can be administered in large mammals such as humans (see col. 4, lines 23-24).

Seiler et al. does not specifically teach a method of treating one or more withdrawal symptoms.

Murray, however, teaches that amphetamines is accompanied by withdrawal effects and can produce depression (pg. 228, 4th paragraph and pg. 230, 2nd and 3rd paragraphs). Murray further teaches that complete discontinuation of amphetamines leads to clinical depression (pg. 230, 4th paragraph).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Seiler et al. with the knowledge of withdrawal effects provided by Murray since chronic abuse of amphetamines. Given that Seiler teaches a method of treating drug abuse and Murray discloses that chronic use of amphetamines is accompanied by withdrawal effects, one of ordinary skill would have been motivated to utilize the method of Seiler et al. with the disclosure of Murray in the treatment of withdrawal effects with the expectation of providing a successful method treatment that is efficacious in treating deleterious symptoms in patients.

Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seiler et al. (U.S. 7,012,085 B2) in view of Murray (J. of Psych. 1998, Vol. 132, No.2, pgs. 227-237) as applicable to claims 1-2 and 6-8 above and in further view of Ward et al. (The Lancet, 1999, Vol. 353, pg. 221-226).

The Seiler and Murray references are as discussed above and incorporated by reference herein. However, Seiler and Murray do not address discontinuing the use of the at least one psychostimulant or gradually reducing the at least one psychostimulant upon administration of the at least one alpha-2-adrenoceptor antagonist.

Ward et al. teaches that in methadone maintenance treatment a substitution of one opioid (i.e. psychostimulant) is used in place of another (i.e. discontinuation of the addictive psychostimulant)and that the goal of most programs is toward abstinence (i.e. complete discontinuation of drugs vs. instant claim 4) from all opioid drugs (see pg. 221, Methadone Maintenance Treatment Section). Ward further teaches that abrupt cessation of methadone often results in a characteristic withdrawal syndrome and that detoxification from MMT is best achieved by a slow reduction in the dose of methadone administered (see instant claim 5 vs. pg. 223, Duration and Withdrawal from MMT Section, 2nd paragraph).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Seiler in view of the knowledge of drug administration provided by Ward et al. to arrive at the method of applicant given that

MMT treatment has long been the standard treatment in drug addiction. Given that Seiler teaches a method of treating drug abuse, and Murray discloses that drugs such as amphetamines are accompanied by withdrawal effects, and Ward discloses a proven method of administration for opioid addiction, one of ordinary skill would have been motivated to utilize the method of Seiler et al. with the disclosures of Murray and Ward with the expectation of providing a method that is effective and successful in treating withdrawal symptoms.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seiler et al. (U.S. 7,012,085 B2) in view of Murray (J. of Psych. 1998, Vol. 132, No.2, pgs. 227-237) as applicable to claims 1-2 and 6-8 above and in further view of Sallinen et al. (Journal of Neuroscience, 1998, Vol. 18, No. 8, pg. 3035-3042, already cited by applicant and filed with an IDS 1449).

The Seiler and Murray references are as discussed above and incorporated by reference herein. However, Seiler and Murray do not address the use of atipamezole as the at least one alpha-2-adrenoceptor antagonist.

Sallinen et al. teaches the use of atipamezole, an alpha-2-adrenoceptor antagonist on behavior paradigms (see abstract and instant claim 10). Importantly, Sallinen et al. reveals that alpha-2c-adrenoceptor antagonist can modulate the startle reflex and its prepulse inhibition and aggressive in mice and implicates atipamezole as

a potential target for the alpha-2c subtype receptor. Sallinen further discloses that these antagonists may have therapeutic value in the treatment of drug withdrawal symptoms.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Seiler et al. with atipamezole to arrive at the method of applicant given that atipamezole may be selective for alpha-2c-adrenoceptors and may be involved in drug withdrawal symptoms. Given that Seiler teaches a method of treating drug abuse and Murray teaches that amphetamine use can lead to withdrawal effects, and Sallinen et al. teaches the use of atipamezole for drug withdrawal symptoms, one of ordinary skill would have been motivated to utilize atipamezole compound of Sallinen et al. in the method of Seiler with the expectation of obtaining a method that is specific in its treatment of withdrawal symptoms.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SJL

12/18/2007

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614